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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/661,927	09/14/2000	William J. Dower	019282-000110US	1158
20350	7590	01/19/2006	EXAMINER	
TOWNSEND AND TOWNSEND AND CREW, LLP			EPPERSON, JON D	
TWO EMBARCADERO CENTER			ART UNIT	
EIGHTH FLOOR			PAPER NUMBER	
SAN FRANCISCO, CA 94111-3834			1639	

DATE MAILED: 01/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/661,927	Applicant(s) DOWER ET AL.	
	Examiner Jon D. Epperson	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-77 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,14,25-29,49,56 and 66 is/are rejected.
- 7) ☒ Claim(s) 15,16,30-35,37,40,46-48,50,52-54,58 and 68 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Continuation of Disposition of Claims: Claims withdrawn from consideration are 4-13,17-24,36,38,39,41-45,51,55,57,59-65,67 and 69-77.

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/21/05 has been entered. Claims 1 and 3-77 were pending. Applicants amended claim 1. No claims were added or canceled. Therefore, claims 1 and 3-77 are currently pending. In addition, claims 4-13, 17-24, 36, 38, 39, 41-45, 51, 55, 57, 59-65, 67 and 69-77 are drawn to non-elected species and/or inventions and thus these claims remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), there being no allowable generic claim. Therefore, claims 1, 3, 14-16, 25-35, 37, 40, 46-50, 52-54, 56, 58, 66 and 68 are examined on the merits in this action.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

Withdrawn Objections/Rejections

2. All rejections are withdrawn in view of Applicants' amendments and/or arguments.

New Rejections

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the

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basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1 and 3, 14, 25-29, 49, 56 and 66 are rejected under 35 U.S.C. 102(b) as being anticipated by Swanson et al. (Swanson, S. J.; Bethke, P.; Jones, R. L. "Barley Aleurone Cells Contain Two Types of Vacuoles: Characterization of Lytic Organelles by Use of Fluorescent Probes" *The Plant Cell* May 1998, 10, 685-698) as evidenced by Ozkan et al. (Ozkan P.; Mutharasan, R. "A rapid method for measuring intracellular pH using BCECF-AM" *Biochim. Biophys. Acta*. 2002, 1572, 143-148).

For *claims 1, 56 and 66*, Swanson et al. (see entire document) disclose the use of a library of fluorescent conjugates in screening and/or characterizing two forms of vacuoles, protein storage vacuoles and secondary vacuoles, in protoplasts of barley aleurone (e.g., see Swanson et al., abstract; see also Table 1), which anticipates the claimed invention. For example, Swanson et al. disclose providing a library comprising different complexes, each complex comprising a compound and a reporter, the compound varying between different complexes (e.g., see Table 1). For example, Swanson et al. disclose the use of BCECF-AM and ZFR-CMAC-GS (e.g., see Table 1, see also figure 4; see also pages 687-688) wherein the different compound represents the "AM" or "ZFR" portions and the reporter represents the cleaved "BCECF" or the "CMAC-GS" (e.g., see figure 4; see also Table 1; see also figure 3; see also discussion; see also Ozkan et al., poage 143, column 2, paragraph 1, disclosing cleavage mechanism for BCECF-AM, "... intracellular esterases cleave the ester bond releacing BCECF, which fluoresces

according to the intracellular pH”). Please note that many other compounds can fall within the scope of the library like the glutathione/sulfhydryl conjugates (e.g., see Table 1). In addition, providing a population of living barley aleurone cells, one or more of which expresses one or more carrier-type transport proteins including organic anion transporter and glutathione conjugate transporter (e.g., see abstract wherein cells are disclosed; see also page 686, column 1, last paragraph; see also page 695, column 1, paragraph 2, “we conclude that at least two kinds of ATP-dependent transporters are present in protein storage vacuoles. One of these is an organic anion transporter that can be inhibited by probenecid and transports BCECF. The other is a glutathione conjugate transporter that is not inhibited by probenecid and transports MCB-GS. Both transporters may belong to the superfamily of ABC transporters”). In addition, the cells were contacted with the library members (e.g., see figures showing uptake of various conjugates). Furthermore, Swanson et al. disclose detecting a signal from the reporter of a complex while internalized within a cell, wherein the reporter preferentially generates the signal once the reporter is internalized within a cell rather than from complexes binding to the surface of the cell, the signal thus providing an indication that a complex whose reporter generated the signal comprises a compound that is a substrate for a carrier-type transport protein (e.g., see figure 4 showing preferential generation of signal for proteolytically cleaved ZFR-CMAC-GS; see also discussion with regard to ZFR-GMAC-GS and conclusion identifying this compound as a substrate for a glutathione conjugate transporter that is a member of the ABC superfamily e.g., see page 695, column 1, paragraph 1). In addition, Swanson et al. disclose that the fluorophores is

linked to a quencher by a linker susceptible to cleavage within the cell, whereby the quencher quenches fluorescence from the fluorophores outside the cell and is cleaved from the fluorophores within the cell after the complex is internalized within the cell, whereby the reporter preferentially generates the signal once internalized within the cell (e.g., see figure 4 showing preferential cleavage of ZFR-GMAC-GS to GMAC-GS wherein a signal is preferentially generated upon internalization; see also Ozkan et al., page 143, column 2, paragraph showing that BCECF-AM is cleaved to BCECF for signal generation upon internalization of BCECF-AM into the cell; see also figures in Swanson et al. showing results of conjugate uptake).

For *claims 3 and 14*, Swanson et al. disclose the enzymatic cleavage of ZFR-CMAC-GS to GMAC-GS substrates (e.g., see figure 4; see also page 688, column 1, last paragraph; see also Ozkan et al., page 143, column 2, paragraph 1).

For *claims 25-28*, Swanson et al. disclose both protein storage and lysosome-like secondary vacuoles, which can be considered a population of cells or, alternatively, the population of cells is differentiated by the addition of (e.g., see figures 1 and 4 showing hormone treatments) or, alternatively, the cells are different based on the addition of various inhibitors and compared to as compared to a control cell wherein the identity of various cells is determined by microscopy (e.g., see figure 9).

For *claim 29*, Swanson et al. disclose cells with different cellular morphologies (e.g., see figure 1 showing differentiation of morphology of protein storage vacuoles versus secondary vacuoles; see also page 686, column 2, last paragraph).

For *claim 49*, Swanson et al. disclose, for example, an organic anion transporter

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(e.g., see page 695, column 1, paragraph 2).

Allowable Subject Matter

4. Claim 15, 16, 30-35, 37, 40, 46-48, 50, 52-54, 58 and 68 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.

January 8, 2006

Jon Epperson
